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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US86/01609 (22) International Filing Date: 4 August 1986 (04.08.86) (31) Priority Application Number: 768,895 (32) Priority Date: 23 August 1985 (23.08.85) (33) Priority Country: US (71) Applicant: WASHINGTON RESEARCH FOUNDATION [US/US]; 1107 N. E. 45th Street, Suite 322, Seattle, WA 98105 (US). (72) Inventors: RATNER, Buddy, D. ; 17015 Dayton Avenue N., Seattle, WA 98133 (US). MATEO, Nancy, B. ; 4520 36th Avenue Northeast, Seattle, WA 98105 (US).		(74) Agents: BIEBER, James, B. et al.; Seed and Berry, 6300 Columbia Center, Seattle, WA 98104-7092 (US). (81) Designated States: AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: POLYMERIC INTRAOCULAR LENS MATERIAL HAVING IMPROVED SURFACE PROPERTIES (57) Abstract An improved intraocular lens material which includes a polymer or glass substrate modified by a gas plasma deposition of a fluorocarbon coating producing a rigid, low-energy surface having significantly reduced cell damage with respect to corneal endothelial tissues. The preferred lens material is produced by exposing a polymeric substrate to a gas plasma of a fluorinated carbon.		

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DescriptionPOLYMERIC INTRAOCULAR LENS MATERIAL HAVING
IMPROVED SURFACE PROPERTIESTechnical Field

The field of the invention is biocompatible polymeric materials. More particularly, the invention relates to such polymers having modified surface properties that substantially improve suitability for intraocular implants.

Background of The Invention

Adhesive contact between the most commonly used intraocular lens material, poly (methyl methacrylate) (PMMA), and the corneal endothelium during surgical implantation results in the loss of endothelial cells which do not regenerate. Cell loss has been directly related to the number of times the intraocular lens contacts the endothelium during surgery, with approximately 20% loss resulting from each contact. The relationships between cell adhesion and polymer surface properties such as surface energy, surface chemistry and surface rigidity have been studied by many investigators. However, corneal endothelial cell adhesion has not been heretofore directly correlated with the properties of the intraocular lens materials examined.

Surface modification of the PMMA surface substrate has been shown to alter lens adhesiveness to cells. Investigators have used gamma radiation grafting to polymerize hydroxyethyl methacrylate (HEMA) and vinyl pyrrolidone (VP) onto a PMMA substrate. Using a laboratory "touch test" between the modified lens material and rabbit corneas, it was discovered that PMMA alone induces 10-30% damage, a PMMA/HEMA graft about 10% damage and a PMMA/VP graft less than 10% cell damage. However, these "touch

tests" have been discovered to be relatively arbitrary and nonreproducible.

Another investigator used an 18 gram weight to press sample intraocular lens and rabbit cornea together for 10 seconds to produce a consistent force on the endothelium. It was reported that PMMA caused "considerable damage", silicone resin lenses induced "less damage" than PMMA, and silicone elastomer created "far less damage". No quantitative comparisons of cell damage between the samples were possible.

In yet another study, the investigator constructed and employed an instrument directly measuring the force of adhesion between rabbit corneal endothelium and intraocular material samples. The average stress calculated for PMMA was 0.66 g/cm^2 which was shown to be the highest of all materials studied. A plasma-deposited VP coating on PMMA and a conventional coating of Healon[™] (manufactured by Pharmacia Inc.) on PMMA each lowered the stress to 0.19 g/cm^2 . Two hydrogels poly (HEMA) and Duragel[™] (Soflex), exhibited the lowest stresses, 0.09 and 0.14 g/cm^2 respectively of the materials tested.

Thus, prior workers have modified PMMA surface properties by coating with a number of materials such as HEMA and VP. They have discovered that such coatings reduce cell damage to values below that measured for the conventional PMMA intraocular lens material. The best state-of-the-art coatings appear to result from surfaces that are soft, hydrophilic hydrogels.

Hydrogels such as HEMA and VP demonstrate low cell damage relative to the PMMA substrate and other coatings tried. However, the hydrogels exhibit a number of disadvantages. For example, the coatings are soft and easily damaged. They are difficult to package and difficult to hydrate properly at surgery. Further, hydrogels are prone to calcification and bacterial contamination.

Disclosure of the Invention

It is an object of the invention to provide a surface-modified polymer that has improved biocompatibility. It is particularly, an object of the invention to provide a
5 surface modified poly (methyl methacrylate) intraocular lens that causes a reduction in adhesion damage of corneal endothelium cells during surgical implantation.

It is an object of the invention to provide an improved, modified intraocular lens material which includes
10 a rigid, low-energy surface having reduced adhesion characteristics with corneal cells.

The improved intraocular lens material of the invention is an intraocular lens material polymer substrate including a fluorocarbon polymer coating bound covalently
15 to the substrate. The fluorinated coating will protect the lens from degradation by the body by virtue of the dense and impermeable cross-linked nature of the film coating. Also, the fluorinated film will protect leaching of fusible components from the lens into the body.

The preferred intraocular lens material is a poly
20 (methyl methacrylate) substrate including a fluorocarbon polymer coating. The surface coating is deposited by exposing the substrate polymer to a gaseous monomer and an electrical field. The field ionizes the monomer gas, creating a fluorocarbon plasma. The plasma reacts with the
25 polymer substrate resulting in the simultaneous deposition and polymerization of the fluorocarbon groups and their attachment onto the substrate surface.

The preferred process for making a modified poly-
30 meric intraocular lens material includes placing poly (methyl methacrylate) substrate material in a chamber including a gaseous perfluoropropane monomer. A radio-frequency generator then induces an oscillating electric field within the chamber polymerizing the monomer and
35 attaching it to the surface of the substrate. System parameters such as RF power, system pressure and length of

reaction control the nature and depth of the deposition as desired.

Brief Description of the Drawings

5 Figure 1 is a schematic diagram of an instrument for contacting treated intraocular lens material with corneal tissue.

 Figure 2 presents percent corneal cell damage as a function of initial force of contact with tested intra-
10 ocular lens materials.

Best Mode for Carrying Out the Invention

 The surface modified intraocular lens material of the invention was produced by coating disks of a substrate
15 polymer, poly (methyl methacrylate), with a fluorocarbon material. In the preferred process, deposition was accomplished by exposing the substrate to a gas plasma of perfluoropropane.

 The plasma reactor was of conventional design
20 including a glass chamber for holding the substrate material to be treated. The chamber was surrounded by capacitance plates coupled to a radio frequency generator which established an oscillating electric field within the chamber.

25 In operation, the sample disks of substrate material were placed in the chamber. The samples were then etched by exposure to an argon plasma. The samples were then exposed to a plasma of the monomer to be deposited on the substrate surface. In addition to the perfluoropropane
30 monomer of the invention, tests were run using ethylene oxide (EO), N-vinyl-2-pyrrolidone (NVP) and hydroxyethyl methacrylate (HEMA). System parameters of RF power, chamber pressure and reaction time were varied to control the nature of the reaction and depth of depositions. Para-
35 meters selected depended upon the character of each monomer tested.

The resulting products were characterized in terms of surface chemistry and surface energy. Cell damage resulting from contact of the sample of the material of the invention with corneal tissue was measured and compared
5 with the untreated substrate and other treated surfaces. The measured surface characteristics of the material of the invention as a function of cell damage were compared with measurements of the same qualities for the other surfaces.

Electron Spectroscopy for Chemical Analysis
10 (ESCA) was used to determine elemental composition and bonding states of the outermost 100 Angstroms of the polymer surface. A survey scan at 1-1000 eV was taken to determine the various elements present. Then, scans in specified eV ranges were made to obtain the spectra of the elements C,
15 O, F and N.

As a means of characterizing the surface energy of the material of the invention and comparable materials, the "critical surface energy" was determined using the method of Zisman, as described in "Relation of the Equili-
20 brium Contact Angle to Liquid and Solid Constitution", Advances in Chemistry Series No. 43, Fowkes, Editor, American Chemical Society, Washington, D.C. pp. 1-51 (1964). The analysis required measuring contact angles of various purified liquids on each type of surface at atmospheric condi-
25 tions. Cosines of the measured angles were then plotted as a function of the surface tensions of the test liquids, resulting in a Zisman plot from which the critical surface energy was calculated.

Actual interaction of the modified surface of the
30 invention with corneal endothelium was determined by employing an apparatus which produced consistent and quantitatively comparable results between samples.

Referring to Figure 1, the device used in this test is shown schematically. A disk 10 of the material to
35 be tested is secured in a holder 11 mounted on the lever arm 12 of a microforce detector 17. A freshly excised rabbit cornea 13 is mounted in a holder 14 on a base 15

opposed to the disk 10 to be tested. A micrometer 16 is provided to advance the lever arm 12 and, the disk sample 10 into contact with the corneal button 13 at a measurable force. An electronic circuit of the microforce detector 17
5 measures the contact force, reporting the measurement on a chart recorder 18.

In operation the test disk 10 was brought into contact with the corneal tissue by means of the micrometer 16 for a period of 40-60 seconds. The initial maximum
10 force under which contact was made was recorded. The corneal buttons were then removed, stained and examined under a low power microscope. The percent damaged cells were counted and recorded.

The details of the process and results achieved
15 are reported in the following examples.

Example 1 PMMA lens material, PERSPEX[™] fabricated by CooperVision of Seattle, Washington, in the form of 10mm diameter disks was selected. Monomers of perfluoropropane and ethylene oxide both manufactured by Matheson
20 Chemical Company of Newark, California, N-vinyl-2-pyrrolidone manufactured by Alfa Products of Danvers, Massachusetts and hydroxyethyl methacrylate manufactured by Hydron Industries were prepared.

25 Sample disks were placed approximately 6cm downstream of the capacitance plates and the continuous system was evacuated at 0.035 Torr. Argon was introduced at 0.25 Torr. RF generator power at 50 watts was continued for five minutes to allow etching of the PMMA substrate. After
30 evacuating the reactor, the fluorocarbon monomer gas was introduced at the desired pressure. For perfluoropropane monomer pressure was 0.25 Torr and generator power was at 30 watts for 10 minutes. Afterwards, the chamber was evacuated to 0.035 Torr and then gradually brought up to
35 the atmospheric pressure by introduction of Argon and air.

Two ESCA spectrometers, a Hewlett Packard Model 5950-B at University of Utah and a Surface Science Model

SSX-100 at University of Washington were used to determine the chemical nature of the surfaces of the intraocular lens material samples. Spectra from the HP-5950-B were resolved using a DuPont 310 curve resolver, while spectra from the
5 SSX-100 were resolved with a peak-fitting routine on an HP-9836-C computer. The C(1s) hydrocarbon peak was assigned to 285eV and used as a reference peak to correct for any energy shifts. The ESCA results of the samples measured appear in section 2 of the following table.

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TABLE 1 Elemental and Bonding Ratios

1. Stoichiometry based on monomer structure

5	Compound	C/O	C/N	C/F	CH	C-O	C=O	O	O	
								"	"	
	PMMA	2.5	-	-	60	20	-	20	-	-
	HEMA	2.0	-	-	50	33.3	-	16.7	-	-
10	NVP	6.0	6.0	-	50	-	-	-	33.3	16.7
	Ethylene Oxide	2.0	-	-	-	100				
						CF ₃	CF ₂	CF ₂ CF _n	CF	C-CF _n
	Perfluoropropane	-	-	0.375		33.3	33.3	-	33.3	-

15 2. ESCA Results

20	Compound	C/O	C/N	C/F	CH	C-O	C=O	O	O	
								"	"	
	PMMA	3.0	-	-	58	23	-	19	-	-
	pHEMA (a)	2.4	-	-	46	38	-	16	-	-
	HEMA (b)	2.2	-	-	46.5	31	-	23.5		
	pNVP (c)	8.0	8.0	-	43.2	-	-	-	29.7	27.1
	NVP (b)	5.7	3.1	-	53	-	-	-	34	13
25	Ethylene Oxide (b)	4.8	-	-	61	21	9	9	-	-
						CF ₃	CF ₂	CF ₂ CF _n	CF	C-CF _n
	Perfluoropropane (b)	-	-	0.52	4.0	28.0	27.6	15.6	13.3	11.5

30 Notes

- (a) Poly(HEMA) spun on glass coverslips (2% in DMF).
 (b) Plasma-deposited film on PMMA disk.
 (c) Poly(NVP) spun on glass coverslip (2% in methanol).

35 The contact angles of various purified liquids on each type of surface were measured under atmospheric conditions using a Rame-Hart goniometer, Model 110-00-00NRL

Experimentally determined values of the critical surface energy γ_c , for the several surfaces tested are presented in Table II. Teflon[™] and Mylar[™] were examined as reference surfaces.

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TABLE II

Critical Surface Tensions (γ_c) of Solid Surfaces

10	Surface	γ_c (ergs cm ⁻²)
	Teflon [™] (TFE)	20.0 \pm 1.3
	Mylar [™]	46.7 \pm 0.3
	PMMA	37.8 \pm 3.2
15	Perfluoropropane film	8.1 \pm 3.1
	Ethylene Oxide film	45.4 \pm 2.7
	HEMA film	49.4 \pm 4.1
	NVP film	48.0 \pm 4.3

20 Example 2

The samples produced and characterized in Example 1 were contacted with corneal tissue by means of the apparatus of Figure 1.

Each cornea, rimmed by 2-3 mm of sclera, was
 25 excised from a 2-3 kg New Zealand white rabbit and immediately placed in RPMI 1640 media with HEPES buffer, L-Glutamine, and penicillin-streptomycin (Grand Island Biological). The cornea in solution was placed in a Forma Scientific Hydrojac CO₂ incubator for at least 30 minutes.
 30 In preparation for a test, the cornea was removed from this solution, rinsed in a 0.9% NaCl solution, placed on a concave Teflon[™] block, and trephined to form a 9-mm-diameter button. The cornea was then placed endothelial side up, in a convex stainless steel holder of the apparatus of Figure
 35 1. A circle of endothelium 7 mm in diameter was exposed with the center projected 2 mm above the level of the holder edge. A 0.9% NaCl solution was dropped intermit-

tently onto the cornea to keep the cells continuously moist.

A 10-mm-diameter sample disk was mounted in the stainless steel holder of the apparatus which clamped the edges, leaving a 9-mm-diameter exposed planar surface. This holder was then attached to the micro-force detector 12, Deflection Sensor Cartridge, Model DSC3, manufactured by Imperial Controls. The system was calibrated using 1-20 gram weights, depending on the force anticipated for each test. The test range was: 4000-20,000 dynes.

The corneal holder was placed directly beneath the lens sample, and the two surfaces were brought into contact with the micrometer attachment. After 40-60 seconds, the cornea and the sample were separated. The cornea was immediately placed in a 0.9% NaCl solution. The initial and maximum force with which contact was made was recorded. Controls for the test were corneal buttons which remained in the holder for 20 minutes and were kept moist with 0.9% NaCl solution. These corneas were subjected to all handling except for actual contact with a sample disk.

To inspect the endothelium, the staining method of Spence and Peyman, described in "A New Technique for the Vital Staining of The Corneal Endothelium," Invest. Ophthalmol, 15, No.12 (1000) 1976, involving a combination of Trypan Blue and Alizarin Red S stains provided by Sigma Chemical of St. Louis, Missouri was used. The cornea was then examined under a low power X100 microscope. A central 9 cm² area, divided into 900 grids, was observed consistently for each cornea. The undamaged and damaged cells were counted.

The PMMA substrate and the treated disk were measured for cell damage over a range of contact forces. The results were then plotted showing cell damage as a function of contact force. Table III reports the best fit curves for the data for each sample. The data are also plotted in Figure 2.

TABLE III
Best Fits for Cell Damage Data

	Surface	Slope	Intercept	Average
5	PMMA	0.00190 ± 0.000494	-1.65 ± 5.4	-
	HEMA	0.000498 ± 0.000190	1.99 ± 2.2	-
	NVP	0.000646 ± 0.000239	1.27 ± 2.7	-
	Ethylene Oxide	0.001240 ± 0.000565	17.44 ± 6.1	-
10	Perfluoro- propane	-	-	6.96 ± 3.83

Referring to Table I of Example 1, the ESCA results of both conventional and plasma deposited polymers are compared with stoichiometry of the monomers. The untreated PMMA disk exhibits C/O ratios close to the expected ratio from stoichiometry. The types of bonding present in the sample also compare closely. Each of the HEMA and NVP plasma-deposited coating shows a close resemblance in composition and bonding to the stoichiometry and to the model poly(HEMA) and poly (NVP) conventional films spun on glass. The peaks comprising the ESCA spectra of the conventional HEMA and NVP polymer surfaces are more distinct than those in the spectral envelopes of the plasma-deposited films. The more ill-defined spectra of the plasma-deposited films reflect the wider distribution of structures, the increased number of chemical species, and the increased crosslinking, all of which are characteristic of plasma depositions. However, the similarity of these plasma deposits to the conventional polymers may indicate a higher level of molecular polymerization (i.e. free radical polymerization through the double bond) than atomic polymerization. This similarity also suggests a comparable regularity of structure which is important to the hydrogel character of conventional poly(HEMA) and poly(NVP). Hence, the coatings deposited by the HEMA and NVP plasma exhibit hydrogel behavior.

Coatings deposited by ethylene oxide and perfluoropropane plasmas are vastly altered from the monomer structures. These plasmas undergo complex reactions involving "atomic polymerization", a type of deposition in which the molecular structure of the monomer is not retained in the polymer. As a result, a regularity in the structure of the ethylene oxide plasma coating is not likely to occur because the bonding environments noted by ESCA are so dissimilar to those in conventional poly-(ethylene oxide).

Referring to Table II of Example 1, the plasma-altered surfaces exhibit definite changes in wettability compared to the PMMA substrate. The fluorinated plasma rendered the disk nonwetable. The other three plasma-deposited surfaces show an increase in wettability as the critical surface tension increases. These results are consistent with the trends reported in the literature, to the effect that wettability decreases with an increase in fluorination and increases with an increase in nitrogen or oxygen bonded to carbon.

In Figure 2, percent cell damage is plotted as a function of initial force for each type of surface contacted with corneal tissue by means of the apparatus shown in Figure 1 and described in Example 2. The solid horizontal line at $3.5 \pm 2.7\%$ represents the average damage associated with the control corneas. The lines shown for the other samples are the best curves for the force-damage data, representing either a least squares fit or an average of cell damage where damage appears independent of force. Table III reports the parameters and errors of the fits of these data.

The choice of fit was based on results from the "f test for chi-square" which determines whether adding a term dependent on force (least squares line) is an improvement from the average damage line. PMMA, ethylene oxide, NVP and HEMA surfaces displayed a trend of increasing damage with increasing force, and the least squares fits were plotted. Since the slope of the perfluoropropane

force-damage curve was not significantly different from zero, the average cell damage value was plotted.

The parameter values shown in Table III were used to calculate the significance of the differences in the cell adhesion associated with the five surfaces. Relative to PMMA, each of the four data sets was found to have greater than 97% probability that the difference between the fit for PMMA and for an altered surface fit is significant.

The fluorinated surface of the invention induced the lowest endothelial damage over the entire force range investigated. Damage appears to be independent of force.

The HEMA and NVP surfaces were also associated with decreased cell damage, compared to the unmodified PMMA. However, both HEMA and NVP surfaces induced increasing cell damage with increasing force. The ethylene oxide coating caused significantly greater adhesion damage to the cornea than PMMA.

As shown, the degree of cell adhesion damage is significantly changed by modifying the PMMA surface. Changes in the surface chemistry and surface energy have been documented by the ESCA and contact angle studies reported in Example 1.

In summary, the data demonstrate a change in surface properties of poly (methyl methacrylate) material modified by RF plasma deposition. The degree of endothelial cell adhesion to the surface is considerably altered. The percent cell damage as a function of the initial force of contact for each modified surface was significantly different than that induced by PMMA. The results suggest that a rigid, low-energy fluorinated surface is desirable for reduced cell adhesion.

Any glass or polymeric substrate for which low-cell adhesion properties are desired and upon which a fluorocarbon monomer may be plasma deposited can be improved by modifying its surfaces according to this invention. Such substrates include glass, poly-propylene and silicone

polymers, for example. Fluorocarbon monomers or mixtures thereof which can be deposited on a substrate using the gas plasma technique are within the scope of the invention. Preferred monomers include perfluoropropane, perfluoropropene, hexafluoroethane, and tetrafluoroethylene, for example.

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Claims

1. An improved intraocular lens material which causes low corneal endothelial cell damage, comprising:
 - a substrate selected from the group consisting of glass and a polymeric material; and
 - a fluorocarbon polymer coating bound covalently to said substrate.
2. The lens material of claim 1 wherein said polymer substrate is poly (methyl methacrylate).
3. The lens material of claim 1 wherein said fluorocarbon polymer coating is a fluorinated hydrocarbon.
4. The lens material of claim 1 wherein said fluorocarbon polymer coating is perfluoropropane.
5. The lens material of claim 1 wherein said fluorocarbon polymer is perfluoropropene.
6. An improved intraocular lens material, which causes comparatively low corneal endothelial cell damage, comprising:
 - a poly (methyl methacrylate) substrate; and
 - a surface coating of perfluoropropane, resulting from exposing said substrate to a monomer of perfluoropropane and an electric field which ionizes said monomer, forming a plasma gas of said monomer which polymerizes and covalently bonds to said substrate.
7. The lens material of claim 6 wherein said gas plasma deposition is produced by means of an inductively coupled radio-frequency generated discharge.

8. The lens material of claim 6 wherein said gas plasma deposition is produced by means of a microwave generated discharge.

9. A method of improving intraocular lens material, reducing corneal endothelial cell adhesion, comprising:

selecting a substrate from the group consisting of glass, poly (methyl methacrylate), polypropylene and silicone polymers; and

modifying the surface of said substrate polymer by plasma deposition of a fluorocarbon monomer selected from the group consisting of perfluoropropane, perfluoropropene, hexafluoroethane, tetrafluoroethylene and mixtures thereof,

whereby a rigid, low-energy surface results wherein said contact cell adhesion is substantially reduced from that of said substrate polymer.

-1/1-

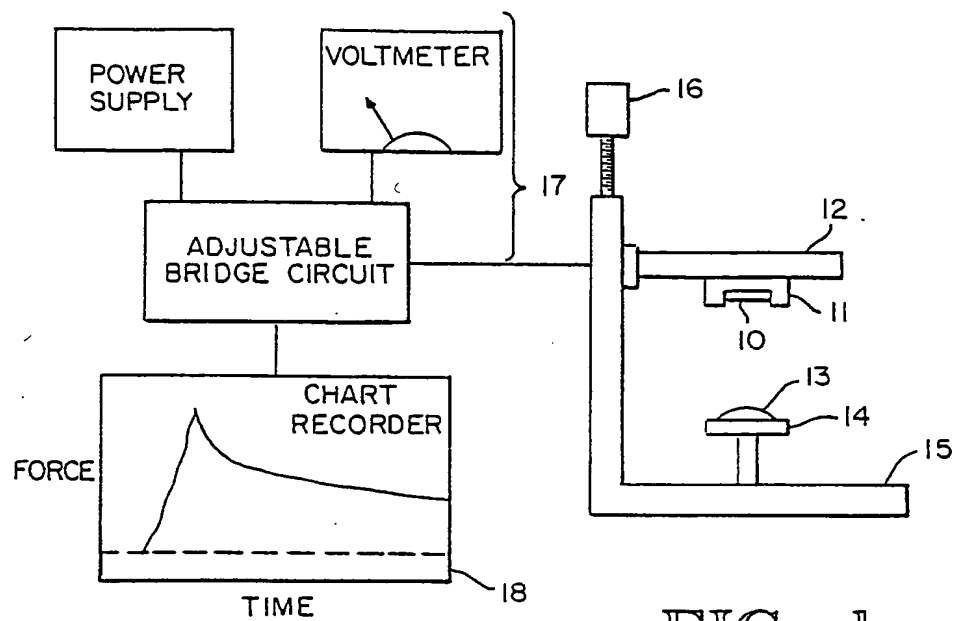
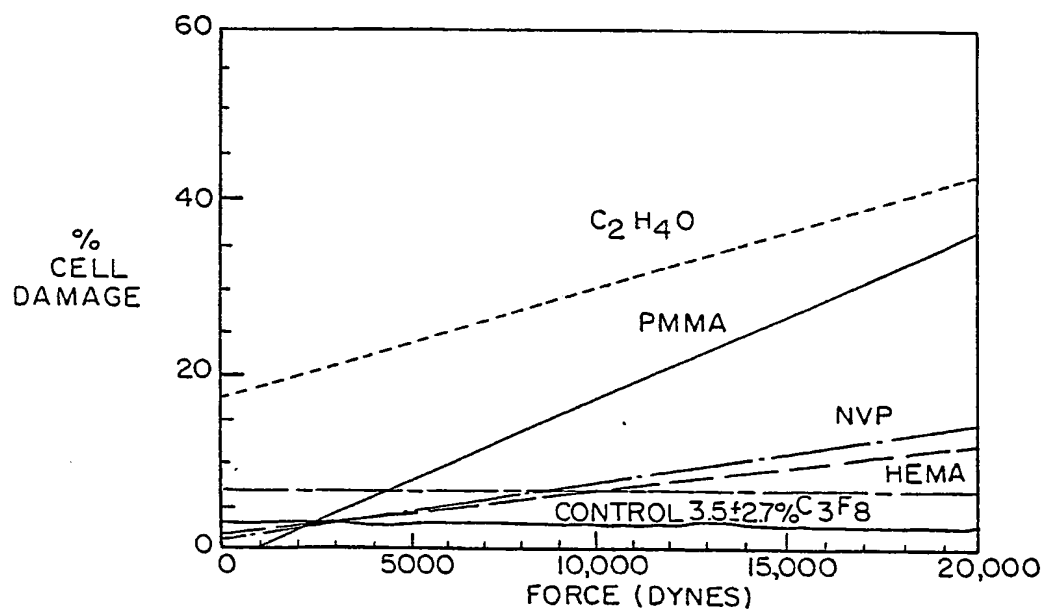


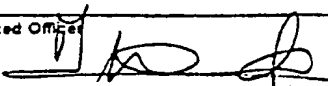
FIG. 1

FIG. 2



INTERNATIONAL SEARCH REPORT

International Application No. **PCT/US 86/01609**

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁴		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC ⁴ : A 61 L 27/00; 33/00; A 61 F 2/16; C 08 J 57/18; G 02 B 1/10		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC ⁴	A 61 F; A 61 L; G 02 B; B 29 D; C 08 J	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
Y	WO, A, 79/00326 (AMERICAN HOSPITAL SUPPLY) 14 June 1979 see claim 1 --	1
Y	WO, A, 79/00327 (AMERICAN HOSPITAL SUPPLY) 14 June 1979 see claim 1 --	1
Y	US, A, 4240163 (M.A. GALIN) 23 December 1980 see claim 1 --	1
Y	US, A, 4312575 (G.A. PEYMAN) 26 January 1982 see claims 1,13,15; column 6, lines 32-66 --	1
Y	CA, A, 473393 (PLASTIC CONTACTLENS COMP.) 15 July 1969 see claim --	1
A	EP, A, 0136807 (EZEKIEL NOMINEES LTD.) 10 April 1985	./.
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>⁹ Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"A" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search 12th December 1986		Date of Mailing of this International Search Report 10 FEB. 1987
International Searching Authority EUROPEAN PATENT OFFICE		Signature of Authorized Officer M. VAN MOL 

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
	see claims 1,2 --	1
A	FR, A, 2328733 (NASA) 20 May 1977 see claims 1,5 --	1
A	Chemical Abstracts, vol. 98, no. 6, 7 February 1983, Columbus, Ohio (US) A. Yamanaka et al.: "Biocompatibility of plastics for intraocular lenses" see abstract 40552, & Afro-Asian J. Ophthalmol. 1982, 1(2), 47-50 -----	1

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON

INTERNATIONAL APPLICATION NO. PCT/US 86/01609 (SA 14255)

This Annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 21/01/87

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		US-A- 4170043	09/10/79
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US-A- 4312575	26/01/82	None	
CA-A- 473393		None	
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